

## **Noadjuvant chemoradiotherapy with 5-fluorouracil-cisplatin combined with cetuximab in patients with resectable locally advanced esophageal carcinoma: A prospective phase I/II trial (FFCD-PRODIGE 3)—Preliminary phase II results.**

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**Background:** Chemoradiotherapy (CRT) for locally advanced esophageal cancer is based on 5FU combined with cisplatin. The anti-EGFR antibody cetuximab increases the efficacy of RT-based regimen for patients (pts) with cancer of the head and neck. This phase I/II trial was evaluating MTD, safety and pathologic complete response (pCR) rate of the combination of cetuximab with platinum-based CRT in esophageal cancer.

**Methods:** Inclusion criteria: squamous cell carcinoma or adenocarcinoma of the esophagus, stage II-III, WHO PS 0-1. A radiotherapy of 45 grays (1.8 Gy/25F) was given over 5 weeks. During phase I, four patients experienced limited toxicity to dose level 0, and treatment was desescalated to dose level -1: weekly cetuximab (400 mg/m<sup>2</sup> one week before start of radiotherapy and 250 mg/m<sup>2</sup> during radiotherapy), and 5 FU (500 mg/m<sup>2</sup> per day D1-D4) combined with cisplatin (40 mg/m<sup>2</sup> D1) on week 1 and 5. Nine pCR over 27 resections were needed to show a pCR rate >20% ( $\alpha=5\%$ , power = 90%). Thirty three patients were included in the phase II.

**Results:** From 07-2007 to 01-2011, 33 pts were enrolled, 20 squamous cell carcinoma (60.6%), 13 adenocarcinoma (39.4%), 25 (75.8%) stage III and 8 (24.2%) stage II. Among 32 pts who received CRT, the main grade 3-4 toxicities were esophagitis (4 pts), leucopenia (1 pt), anaphylaxis reaction (1 pt), rash (1 pt). Resection was achieved in 27 pts (25 R0)/31 who underwent surgery. Complete or near complete pathologic response (TRG grades 1 and 2 to Mandard) was achieved respectively in 5 (18.5%) and 6 (22.2%) pts. There were 4 deaths at 30 days post surgery. Severe postoperative complications were pulmonary complications (8), anastomotic stricture (4), gastric necrosis (1) and infection (7). The median overall survival was 15.7 months [11.01-.], and the median relapse free survival was 13.7 months [5.47-.].

**Conclusions:** Adding cetuximab to preoperative chemoradiotherapy including 5FU and cisplatin did not increase pCR. The recommended dose level of chemotherapy determined during phase I could explain those disappointing results. We won't initiate a phase III trial.